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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,155	12/02/2003	John S. Babcook	ABGENIX.073A	5639

20995 7590 12/19/2005

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EXAMINER	
RINAUDO, JO ANN S	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/727,155	BABCOOK ET AL.	
	Examiner	Art Unit	
	Jo Ann Rinaudo	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 and 40-51* is/are pending in the application.

4a) Of the above claim(s) *39,44,45 and 47-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-38, 40-43, and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

DETAILED ACTION

1. Claims 1-38 and 40-51 are pending.

2. Applicant's election without traverse of Group I (claims 1-43 and 46, now claims 1-38, 40-43, and 46) in the reply filed on 24 October 2005 is acknowledged.

3. Claims 44, 45, 47-51 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Applicant has further elected the species of antibody identified in the application as "299v2" which comprises the heavy chain amino acid sequence shown in SEQ ID NO: 74 and the light chain amino acid sequence shown in SEQ ID NO: 72. Upon reconsideration, Examiner has extended the search to cover the following species, SEQ ID NO: 48, 50, 52, 54, 56, and 70.

5. Claims 1-38, 40-43, and 46 read on the elected species.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth herein. The amino acid sequences recited in Claims 1-3, 6-8, 10-15, 23-25, 27-29, and 31-36 need to comply with the sequence rules.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

8. Claims 16, 17, 37 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In Claims 16, 17, 37 and 38, the use of "VH3-33", "AK0VK1", "VH3-53", and "L2VK3", respectively, renders the claims indefinite because "VH3-33", "AK0VK1", "VH3-53", and

"L2VK3", are laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designation to define completely distinct biological materials.

10. Claims 16, 17, 37 and 38 are vague and indefinite in the recitation of "a human monoclonal antibody" that comprises a "gene". It is unclear how a monoclonal antibody, which is a protein, comprises a gene, which is a nucleic acid.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

12. Claims 1-38, 40-43, and 46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises a heavy chain (SEQ ID NO: 74) and containing CDR1 (amino acids 31-35 of SEQ ID NO: 74), CDR2 (amino acids 50-66 of SEQ ID NO: 74), and CDR3 (amino acids 99-114 of SEQ ID NO: 74); and a light chain (SEQ ID NO: 72) containing CDR1 (amino acids 24-34 of SEQ ID NO: 72), CDR2 (amino acids 50-56 of SEQ ID NO: 72), and CDR3 (amino acids 89-97 of SEQ ID NO: 72) and a composition for said antibody *does not reasonably provide enablement for* a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha which comprises less than 6 CDR's (Claims 1-38, and 40-43 and 46); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises VH3-33 heavy chain gene, or conservative variant thereof (Claim 16); a human monoclonal antibody comprising a VH3-33 heavy chain gene and comprising an A30VK1 light chain gene (Claim 17); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises VH3-53 heavy chain gene, or conservative variant thereof (Claim 37); a human monoclonal antibody comprising a VH3-53 heavy chain gene and comprising a L2VK3 light chain gene (Claim 38); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 (Claim 18); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 and a heavy chain CDR2 corresponding to canonical class 3 (Claim 19); a human monoclonal

antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, and a light chain CDR1 corresponding to canonical class 2 (Claim 20); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, a light chain CDR1 corresponding to canonical class 2, and a light chain CDR2 corresponding to canonical class 1 (Claim 21); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, a light chain CDR1 corresponding to canonical class 2, a light chain CDR2 corresponding to canonical class 1, and a light chain CDR3 corresponding to canonical class 1 (Claim 22); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 and a heavy chain CDR2 corresponding to canonical class 1 (Claim 40); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, and a light chain CDR1 corresponding to canonical class 2 (Claim 41); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, a light chain CDR1 corresponding to canonical class 2, and a light chain CDR2 corresponding to canonical class 1 (Claim 42); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, a light chain CDR1 corresponding to canonical class 2, a light chain CDR2 corresponding to canonical class 1, and a light chain CDR3 corresponding to canonical class 3 (Claim 43); or a composition comprising a human monoclonal antibody, or functional fragment thereof, that specifically binds to Tumor Necrosis Factor-alpha which comprises less than 6 CDR's (Claim 46). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

13. Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d

1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the amount of direction or guidance provided, the lack of sufficient working examples, and the amount of experimentation required to enable one skilled in the art to practice the invention.

14. It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. Janeway et al. teach that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Furthermore, the specification provides no guidance for making an antibody exhibits binding to Tumor Necrosis Factor-alpha other than the human monoclonal Tumor Necrosis Factor-alpha comprising a heavy chain (SEQ ID NO: 74) and containing CDR1 (amino acids 31-35 of SEQ ID NO: 74), CDR2 (amino acids 50-66 of SEQ ID NO: 74), and CDR3 (amino acids 99-114 of SEQ ID NO: 74); and a light chain (SEQ ID NO: 72) containing CDR1 (amino acids 24-34 of SEQ ID NO: 72), CDR2 (amino acids 50-56 of SEQ ID NO: 72), and CDR3 (amino acids 89-97 of SEQ ID NO: 72). Therefore, the lack of guidance provided, the lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to make and use a Tumor Necrosis Factor-alpha antibody, as recited in the instant claims.

15. Claims 16 and 37 recite a "conservative variant thereof". The specification does not disclose ALL the possible variants. Rudikoff teaches that even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect the antigen-binding function. In addition, Rudikoff teaches that an alteration of a single amino acid in the CDR resulted in the loss of antigen-binding function. Furthermore, an antibody requires the association of the complete heavy and light chain variable regions of a given antibody, as discussed supra. Therefore, the lack of guidance provided and the amount

of experimentation required does not enable one skilled in the art to make ANY "conservative variant thereof", as recited in the instant claims.

16. The terms "comprises" and "comprising" in Claims 16, 17, 37 and 38 are open-ended and expand the nucleic acid sequence to include additional non-disclosed nucleic acids outside the given sequence. The specification fails to define the nucleic acid sequences outside the given sequence, the lack of sufficient limitations would therefore allow for ANY nucleic acid sequences outside the given sequence. Given that an antibody requires the association of the complete heavy and light chain variable regions, as discussed supra, the function of the resulting protein would be unpredictable and would not produce a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha. Therefore, the lack of guidance provided and the amount of experimentation required does not enable one skilled in the art to make and use a Tumor Necrosis Factor-alpha antibody, as recited in the instant claims.

17. Claims 18-22 and 40-43 recite a "canonical class". MacCallum et al. teach that the non-contacting residues within the CDRs coincide with the canonical backbone conformations. The side-chains of the canonical key residues pack internally and make few antigen contacts (see page 735, column 1, paragraph 1, in particular). Furthermore, Vargas-Madrazo et al. teach that the majority of antibody seqeuences correspond to only ten canonical structure classes (see page 499, Table 1; and page 500, column 2, lines 1-9, in particular). Therefore, defining an antibody by only the canonical class of one of the complementarity determining regions (CDR) does not provide sufficient enabling disclosure on how to make a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha. Furthermore, an antibody requires the association of the complete heavy and light chain variable regions of a given antibody, as discussed supra. Claims 18-22 and 40-43 do not recite complete heavy and light chain variable regions of a given antibody. Therefore, the lack of guidance provided, the lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to make and use a Tumor Necrosis Factor-alpha antibody, as recited in the instant claims.

18. Claim 46 recites a "functional fragment thereof". The specification does not disclose the definition of a "functional fragment thereof". The broad term "functional fragment thereof"

encompasses ANY functional fragment of the antibody. It is well established in the art that the Fc fragment of an antibody is a functional fragment (activation of complement) but cannot bind an antigen (see Benjamini et al.). Therefore, the use of ANY functional fragment of a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha is unpredictable. Furthermore, an antibody requires the association of the complete heavy and light chain variable regions of a given antibody, as discussed supra. Claim 46 does not recite complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. Therefore, the lack of guidance provided, the lack of sufficient working examples, and the amount of experimentation required does not enable one skilled in the art to use a Tumor Necrosis Factor-alpha antibody "functional fragment thereof", as recited in the instant claims.

19. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. In view of the quantity of experimentation necessary, the lack of working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

20. Claims 1-38, 40-43, and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

21. Applicant is in possession of a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises a heavy chain (SEQ ID NO: 74) and containing CDR1 (amino acids 31-35 of SEQ ID NO: 74), CDR2 (amino acids 50-66 of SEQ ID NO: 74), and CDR3 (amino acids 99-114 of SEQ ID NO: 74); and a light chain (SEQ ID NO: 72) containing CDR1 (amino acids 24-34 of SEQ ID NO: 72), CDR2 (amino acids 50-56 of SEQ ID NO: 72), and CDR3 (amino acids 89-97 of SEQ ID NO: 72) and a composition for said antibody.

22. Applicant is not in possession of a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha which comprises less than 6 CDR's (Claims 1-38, and 40-43 and

46); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises VH3-33 heavy chain gene, or conservative variant thereof (Claim 16); a human monoclonal antibody comprising a VH3-33 heavy chain gene and comprising an A30VK1 light chain gene (Claim 17); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises VH3-53 heavy chain gene, or conservative variant thereof (Claim 37); a human monoclonal antibody comprising a VH3-53 heavy chain gene and comprising a L2VK3 light chain gene (Claim 38); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 (Claim 18); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 and a heavy chain CDR2 corresponding to canonical class 3 (Claim 19); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, and a light chain CDR1 corresponding to canonical class 2 (Claim 20); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, a light chain CDR1 corresponding to canonical class 2, and a light chain CDR2 corresponding to canonical class 1 (Claim 21); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 3, a light chain CDR1 corresponding to canonical class 2, a light chain CDR2 corresponding to canonical class 1, and a light chain CDR3 corresponding to canonical class 1 (Claim 22); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1 and a heavy chain CDR2 corresponding to canonical class 1 (Claim 40); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, and a light chain CDR1 corresponding to canonical class 2 (Claim 41); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1 corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, a light chain CDR1 corresponding to canonical class 2, and a light chain CDR2 corresponding to canonical class 1 (Claim 42); a human monoclonal antibody that specifically binds to Tumor Necrosis Factor-alpha comprises a heavy chain CDR1

corresponding to canonical class 1, a heavy chain CDR2 corresponding to canonical class 1, a light chain CDR1 corresponding to canonical class 2, a light chain CDR2 corresponding to canonical class 1, and a light chain CDR3 corresponding to canonical class 3 (Claim 43); or a composition comprising a human monoclonal antibody, or functional fragment thereof, that specifically binds to Tumor Necrosis Factor-alpha which comprises less than 6 CDR's (Claim 46).

23. There is insufficient written description of an antibody that specifically binds to Tumor Necrosis Factor-alpha and comprises less than 6 specific known CDR sequences or heavy chain (V_H Domain) and a light chain (V_L Domain). The specification does not describe sufficient structural and functional characteristics of an antibody that specifically binds to Tumor Necrosis Factor-alpha, other than the antibody that comprises a heavy chain (SEQ ID NO: 74) and containing CDR1 (amino acids 31-35 of SEQ ID NO: 74), CDR2 (amino acids 50-66 of SEQ ID NO: 74), and CDR3 (amino acids 99-114 of SEQ ID NO: 74); and a light chain (SEQ ID NO: 72) containing CDR1 (amino acids 24-34 of SEQ ID NO: 72), CDR2 (amino acids 50-56 of SEQ ID NO: 72), and CDR3 (amino acids 89-97 of SEQ ID NO: 72). Therefore the skilled artisan cannot envision all the contemplated antibodies that bind to specifically to Tumor Necrosis Factor-alpha, as recited in the instant claims.

24. There is insufficient written description of a "conservative variant thereof", "a canonical class", and a "functional fragment thereof" (Claims 16, 18-22, 37, 40-43, and 46). The specification does not describe sufficient structural and functional characteristics of an antibody that specifically binds to Tumor Necrosis Factor-alpha, comprises less than 6 specific known CDR sequences or heavy chain (V_H Domain) and a light chain (V_L Domain) and is a "conservative variant thereof", "a canonical class", or a "functional fragment thereof." Therefore the skilled artisan cannot envision all the contemplated antibodies that bind to specifically to Tumor Necrosis Factor-alpha, as recited in the instant claims.

25. There is insufficient written description of a human monoclonal antibody that specifically binds to TNF-alpha and "comprises" VH3-33 heavy chain (Claim 16), A30VK1 light chain (Claim 17), VH3-53 heavy chain (Claim 37), or L2VK3 light chain (Claim 38). The specification does not describe sufficient structural and functional characteristics of an antibody that specifically

binds to Tumor Necrosis Factor-alpha and comprises less than 6 specific known CDR sequences or heavy chain (V_H Domain) and a light chain (V_L Domain). Therefore the skilled artisan cannot envision all the contemplated antibodies that bind to specifically to Tumor Necrosis Factor-alpha, as recited in the instant claims.

26. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

27. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

28. Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

29. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

30. No claim is allowed.

31. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jo Ann Rinaudo whose telephone number is 571.272.8143. The examiner can normally be reached on M-F, 8:30AM - 5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571.272.0841. The fax phone number for the organization where this application or proceeding is assigned is 571.273.8300.

32. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jo Ann Rinaudo, Ph.D.
Patent Examiner
12/08/2005

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Continuation of Attachment(s) 6). Other: Notice to comply with Sequence Rules.

Application No.: 10/727,153

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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COPY FOR [ ] File [ ] Applicant